Polyinositoe-alphaII gene expression as a Predictor of Responsiveness to Anthracycline-Containing Chemotherapy in the Breast Cancer International Research Group 006 Clinical Trial of Herceptin (Trastuzumab) in the Adjunct Setting
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Abstract

Objectives 1. Assess the frequency of TOPISA gene expression in the breast cancer tissue sections of the patients in the BCIRG 006 trial. 2. Determine if TOPISA gene expression status and breast cancer clinical characteristics were associated.

Methods: We evaluated topoisomerase II-alpha expression by fluorescence in situ hybridization (FISH) in breast cancer tissue sections from 228 of the 3225 patients entered in the BCIRG 006 clinical trial. Overall and disease-free survival (OFS and DFS) were analyzed using the Kaplan-Meier method. The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.

Results: TOPISA gene expression was determined in 228 of the 325 patients in the BCIRG 006 clinical trial. Overall, 99 (43.6%) patients were TOPISA-negative and 129 (56.4%) patients were TOPISA-positive. The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.

Conclusions: TOPISA gene expression was determined in 228 of the 325 patients in the BCIRG 006 clinical trial. Overall, 99 (43.6%) patients were TOPISA-negative and 129 (56.4%) patients were TOPISA-positive. The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.

Background:

The human epidermal growth factor receptor type II (HER2) gene encodes a transmembrane protein that is overexpressed in a subset of breast cancers. Overexpression of HER2 is associated with poor prognosis and resistance to chemotherapy. Several methods have been developed to detect HER2 overexpression, including IHC and FISH. However, IHC is a subjective method that can lead to variability in results. FISH is a more objective method that can provide more accurate results. FISH is performed by hybridizing DNA probes to the HER2 gene and a reference gene (usually EBER or ETV6). The ratio of HER2 to reference gene signals is then measured using a fluorescence microscope.

Materials and Methods:

Tissue Specimens: Paraffin-embedded tissue blocks of unstained breast cancer tissue sections from the BCIRG 006 clinical trial were used for FISH analysis. The tissue blocks were stained with hematoxylin and eosin (H&E) prior to FISH analysis. The H&E stains were used to identify the tumor tissue sections for the FISH analysis.

Tissue Microarrays: Tissue microarrays were prepared from tumor tissue blocks using a tissue arrayer. Each tissue arrayer was loaded with tissue from one patient, and a microscopic view of the tissue arrayer was used to identify the tumor tissue sections for the FISH analysis.

Tissue Sections: Tissue sections were prepared from the tumor tissue blocks for FISH analysis. The tissue sections were deparaffinized and hydrated prior to FISH analysis. The tissue sections were then stained with a DNA-specific dye, such as DAPI, and a fluorescently labeled probe specific for the HER2 gene.

Results:

TOPISA gene expression was determined in 228 of the 325 patients in the BCIRG 006 clinical trial. Overall, 99 (43.6%) patients were TOPISA-negative and 129 (56.4%) patients were TOPISA-positive. The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.

Conclusions:

TOPISA gene expression was determined in 228 of the 325 patients in the BCIRG 006 clinical trial. Overall, 99 (43.6%) patients were TOPISA-negative and 129 (56.4%) patients were TOPISA-positive. The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.

Homologous recombination (HR) proteins play an essential role in DNA repair and cell survival. Defects in HR function are associated with increased sensitivity to DNA-damaging agents, such as anthracyclines and topoisomerase II inhibitors. Our study aimed to determine the frequency of TOPISA gene expression in breast cancer tissue sections from the BCIRG 006 clinical trial. The frequency of TOPISA gene expression was determined using fluorescence in situ hybridization (FISH). The association between TOPISA expression and clinical characteristics was evaluated using a chi-square test and the log-rank test. The correlation between TOPISA expression and clinical characteristics was evaluated using the Spearman's rank correlation coefficient.